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A room temperature alternative of the Claisen rearrangement route to *ortho* allylated phenols: unique reactivity pattern of allylindium reagents

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Abstract—Quinol ethers and quinone monoketals are shown to undergo formal anti-Michael addition reactions with allylindium reagents at room temperature to give only *ortho* allylated phenols in good yields.

The Claisen rearrangement,[1] viewed as a [3,3] sigmatropic thermal isomerization, is a very useful carbon–carbon bond forming reaction. It has been widely used in the total synthesis of natural products.[2] Since the original report[3] by Claisen in 1912, the reaction has witnessed numerous variants such as Caroll, Ireland, Bellus, etc., which are all related to the aliphatic version of the rearrangement.[1] Surprisingly, there is no literature report on the alternatives of the aromatic Claisen rearrangement route to allylated products. The Claisen route to *ortho* allylated phenols traditionally entails two steps: *o*-allylation of phenols and thermal isomerization of the *o*-allyl derivatives. The rearrangement is typically carried out at 150–300 °C. Although the products of rearrangement are usually *ortho* isomers, *para* allylated phenols and benzofurans are often formed as side products. The rearrangement can be performed at room temperature only when alkylaluminium halides are used as catalysts.[4] However, the requirement for a large excess of highly acidic catalysts restricts the practical uses of this variant. Herein, we report an ambient temperature alternative of the Claisen rearrangement route to *o*-allylated phenols from the same set of starting materials as used in the Claisen route. This is based upon oxidative dearomatization of phenols to quinol ethers or quinone monoketals followed by their formal anti-Michael addition reaction with allylindium reagents. The two-step conversion can be carried out in one operation, by avoiding isolation and purification of the substrates from the crude reaction mixtures if they are prepared by oxidation of the corresponding phenols with phenyliodonium diacetate (PIDA).

In connection with our ongoing programme[5] on the total synthesis of angucyclines, we planned to prepare 5-allyl-4-methoxy-2-cyclohexenones (e.g., **5**) from quinol derivatives,[6] which are accessible via a variety of routes. Since there is no literature report on 1,4-addition of allylmetal reagents to quinol ethers,[7] we envisaged the preparation of compound **5** in two steps (Scheme 1), namely 1,2-addition of an allylmetal reagent to compound **2** and oxy-Cope rearrangement of the resulting product **4**. The proposed tandem methodology is well documented for acyclic systems and quinones.[8] In view of increasing interest in the use of allylindium reagents[9] and the operational simplicity associated with them, we decided to examine the Barbier type reactivity of the parent allylindium reagent **3** towards quinol ether **2** in order to obtain compound **4**.

When compound **2**,[10] prepared by oxidation of *p*-cresol with phenyliodonium diacetate in methanol, was reacted in DMF with the allylindium reagent derived from allyl bromide, a colourless liquid was isolated as the sole product after work-up of the mixture and purification of the crude product by chromatography. It was found to be 2-allyl-4-methylphenol **6**, contrary to the expected product **4** or **5** (Scheme 1). Since both 2-allyl and 3-allyl

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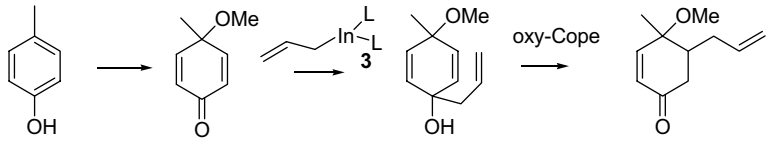
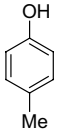
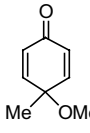
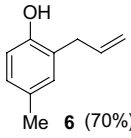
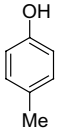
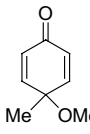
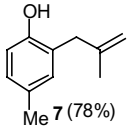
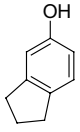
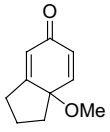
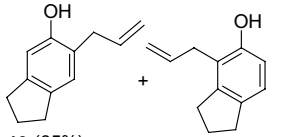
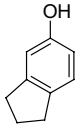
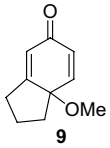
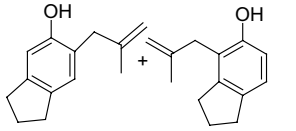
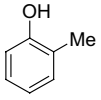
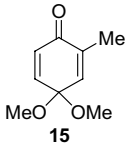
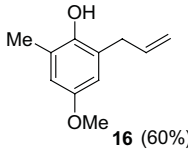
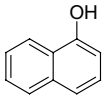
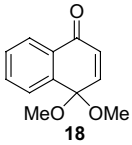
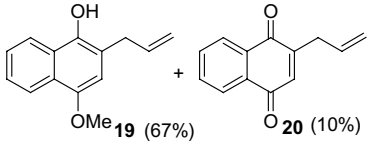
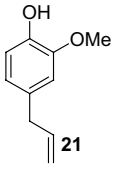
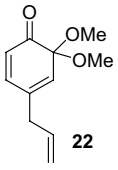
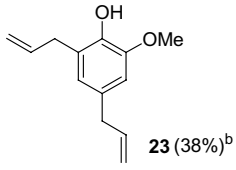


Scheme 1. The proposed route for the preparation of cyclohexenone **5**.

derivatives of 4-methylphenol **1** have very similar ^{1}H NMR spectra, the structure of compound **6** was confirmed by spectroscopic comparison with an authentic sample prepared from *p*-cresol in two steps by the published method.[11] This unusual reactivity of quinol ether **2** prompted us to look into the scope of the reaction and thus several substrates were examined under similar conditions. The results are summarized in Table 1. When the indium reagent derived from 2-methylallyl bromide was examined with quinol ether **2**, the *ortho* allylated phenol **7**[12] was obtained as the sole product in 78% yield. The result with quinol ether **9**[5a] was different as expected. The allyl derivative **10** was formed in 65% yield along with its regioisomer **11** in 14% yield. Though

Table 1. Allylation of quinol ethers and quinone ketals with allylindium reagents[18]

Entry	Phenol	Enone	Metal, allyl bromide	Product (% yield)[a]
1				 **6** (70%) (45%)[b]
2				 **7** (78%)
3	 **8**	 **9**		 **10** (65%) **11** (14%)
4		 **9**		 **12** (70%) **13** (10%)
5	 **14**	 **15**		 **16** (60%)
6	 **17**	 **18**		 **19** (67%) **20** (10%)
7	 **21**	 **22**		 **23** (38%)[b]

[a] Yields are unoptimized and refer to the allylation step.
[b] Yields refer to a one-pot process.